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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/323,597	06/01/99	AFAR D	1703-007.US1

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GATES & COOPER LLP
HOWARD HUGHES CENTER
6701 CENTER DRIVE WEST,
SUITE 1050
LOS ANGELS, CA 90045

EXAMINER	
NICKOL,G	
ART UNIT	**PAPER NUMBER**
1642	22

DATE MAILED: 05/23/01

Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

Offic Action Summary	Application No.	Applicant(s)	
	09/323,597	AFAR ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2001 and 06 October 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 20-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,20-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

Response to Amendment

The Amendment filed October 6, 2000 (Paper No. 15) in response to the Office Action of July 3, 2000 is acknowledged and has been entered. Claims 1-5, and 20-31 are pending. Claims 2-5 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 20-25 were amended. Claims 1 and 20-31 are pending and are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Priority

It is maintained that the priority of the present application is April 14, 1999 for the reasons of record in Paper No. 10, page 3. Although applicants have corrected the identity to Applicant's first provisional application (60/087,598), filed June 1, 1998 (see Paper No. 15, page 4), a review of this application did not reveal the presently claimed amino acid sequences. Additionally, applicants submitted a corrected Sequence Listing to the claimed amino acid sequence (Paper No. 19) prior to the issuance of this Office Action. This was to correct an error in SEQ ID NO: 2 which is now 492 amino acids long (versus 491) as described in the specification as filed (see Paper No. 14). However, as maintained in the previous Office Action, applicant must submit objective evidence of the claimed amino acid sequence where support can be found establishing an earlier priority date.

Specification

The objections to the specification recited in Paper No. 10, page 3 are withdrawn in view of applicant's amendments. Applicants further point out (Paper No. 15, page 5) that the sequence listing designations for Figures 1, 2, and 3 were introduced into the specification in a Preliminary Amendment filed on December 22, 1999. The argument has been considered and is found persuasive.

The brief description of Figure 3 remains objected to for the reasons of record in Paper No. 10, page 4. Applicants argue that upon indication of allowable subject matter, Applicants will correct the drawings as suggested by the Examiner. This argument has been considered, and is persuasive pending corrections by Applicant.

Rejections Withdrawn

The rejection of Claims 20-25 under 35 U.S.C. 101 (because the claimed invention is directed to non-statutory subject matter) is withdrawn in view of Applicants amendments and arguments there to.

Rejections Maintained

Claims 1,20-31 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons of record in Paper No. 10, pages 4-7.

Applicants argue (Paper No. 15, page 6) that useful information (such as information relating to the status of a disease) can be obtained from assays of proteins, even when the biological function of that protein is unknown. Applicants further point to the clinical relevance of assaying Prostate Specific Antigen (PSA) as a marker to monitor the presence and location of prostate cancers and further point out that that little is known about the biologic function of this non-prostate specific molecule. This argument has been considered but is not found persuasive. The utility and art-recognized clinical usefulness of one protein does not extrapolate to the usefulness of a completely distinct protein as claimed by applicant. As further indicated by Fortier et al. (Paper No. 15, attached as Exhibit C), measurements of serum levels of PSA is widely used as a screening tool for prostate cancer (abstract), whereas the disclosure by Applicant, encompassing the TMPRSS2 protein, fails to teach such a well-established utility as that of PSA. Furthermore, the basis of the utility rejection was not wholly directed to the unknown function of TMPRSS2 because the asserted utility of the 20P1F12/TMPRSS2 was further based on the chemical and structural homology of 20P1F12/TMPRSS2 to a previously reported human protein, TMPRSS2 which further had sequence similarity with members of a serine protease family of proteins. However, as detailed in the previous Office Action, demonstration of chemical and structural homology does not provide substantial credibility that the 20P1F12/TMPRSS2 and or fragments thereof will function like TMPRS22, or moreover, as a protease.

Applicants further argue that TMPRSS2 polypeptides having immunoreactive epitopes can be used to generate antibodies for use in assays that are analogous to those which measure PSA. Applicants further argue that TMPRSS2 exhibits specific properties that allow it to be used

to monitor the presence and or location of cancers and or as a potential imaging agent for metastasized disease. This argument has been considered but is not found persuasive. First, asserted utilities for 20P1F12/TMPRSS2, such as the generation of antibodies useful for diagnostic and prognostic assays, imaging methodologies, and therapeutic methods in the management of human cancers such as colon and prostate (page 13, lines 9-22, page 18, line 5) also applies to many *unrelated* polypeptide structure sequences, i.e. PSA, p53 and others. Therefore, the asserted utilities are not considered "specific" utilities since they are not specific to 20P1F12/TMPRSS2. Secondly, applicant has not demonstrated that TMPRSS2 exhibits specific properties that allow it to be used to monitor the presence of cancers. Applicants point to Figure 5 of the specification, however Figure 5 only teaches that *equal* levels of 20P1F12/TMPRSS2 expression were present in both normal prostate and cancerous prostate xenografts (Figure 5). Thus, Applicant's arguments have not been found persuasive and the rejection is maintained.

Claims 1, 20-31 also remain rejected under 35 U.S.C. 112, first paragraph for the reasons above and those made of record in Paper No. 10, page 7. Specifically, since the claimed invention is not supported by either a specific and or well established for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 20-31 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising SEQ ID NO. 2, does not reasonably provide enablement for polypeptides comprising a fragment of the

20P1F12/TMPRSS2 protein as shown in Fig. 1 (SEQ ID NO:2) wherein a valine is at position 160, or a fragment of the 20P1F12/TMPRSS2 protein wherein an isoleucine is at position 242, or a fragment of the 20P1F12/TMPRSS2 protein wherein glutamic acid is at position 329, or a fragment of the 20P1F12/TMPRSS2 protein wherein lysine is at position 449, or a fragment of the 20P1F12/TMPRSS2 protein wherein an arginine is at position 489, or a fragment of the 20P1F12/TMPRSS2 protein wherein aspartic acid is at position 491 for the reasons of record in Paper No. 10, pages 8-10.

Applicants argue that the amendment to the claims to include "wherein the polypeptide fragment comprises an immunoreactive epitope" renders the rejection moot. This argument has been considered but is not found persuasive. This limitation of a fragment comprising an immunoreactive epitope does not perfect the rejection because the claims remain broadly drawn to any and all polypeptide fragments comprising any amino acid which flanks either valine, isoleucine, glutamic acid, lysine, arginine, and or aspartic acid, and applicant has not enabled all of these types of modified proteins because it has not been shown that these modified proteins are capable of functioning as that which is being disclosed.

Applicants further argue that the disclosure teaches one skilled in the art how to make immunogenic polypeptide fragments of TMPRSS2 and how to use these polypeptides to generate antibodies useful in tracking the metastasis of cancer cells. This argument has been considered but is not found persuasive. It is well known in the art that when using synthetic amino acid sequences as immunogens to develop antibodies, one cannot be certain how well exposed such a peptide is nor how immunogenic it is. Furthermore, this does not take into account the 3 dimensional folding of the native molecule, nor its glycosylation or other post-translational

modifications and other characteristics which are of significant importance in an antibody response. Peptides or synthetic antigens cannot effectively substitute for the natural tertiary and quarterary structure of a protein in a physiological situation. Further, there is no teaching in the specification of which part of the protein should be used to produce antibodies which will bind specifically to the broadly claimed TMPRSS2 polypeptides. Moreover, Applicants have not taught how to use antibodies useful in tracking the metastasis of cancer cells for the reasons recited above and for the reasons of record in Paper No. 10, pages 4-7. Thus, Applicant's arguments have not been found persuasive and the rejection is maintained.

New Rejections

Claim Rejections - 35 USC § 102

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, and 20-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Wong et al. (US Patent No. 6,166,194), June 29, 1998.

The claims are drawn to an isolated 20P1F12/TMPRSS2 protein having an amino acid sequence shown in Figure 1 (SEQ ID NO:2) (Claim 1).

The claims are further drawn to a polypeptide comprising a fragment of the 20P1F12/TMPRSS2 protein of Claim 1 wherein a valine is at position 160 and further comprises an immunoreactive epitope (Claim 20); a fragment of the 20P1F12/TMPRSS2 protein wherein an isoleucine is at position 242 and further comprises an immunoreactive epitope (Claim 21); a

fragment of the 20P1F12/TMPRSS2 protein wherein glutamic acid is at position 329 and further comprises an immunoreactive epitope (Claim 22); a fragment of the 20P1F12/TMPRSS2 protein wherein lysine is at position 449 and further comprises an immunoreactive epitope (Claim 23); a fragment of the 20P1F12/TMPRSS2 protein wherein an arginine is at position 489 and further comprises an immunoreactive epitope (Claim 24); a fragment of the 20P1F12/TMPRSS2 protein wherein aspartic acid is at position 491 and further comprises an immunoreactive epitope (Claim 25). The claims further include fragments of the latter comprising an immunoreactive epitope within the protease domain (Claims 26-31).

Wong et al. teach an isolated amino acid sequence which is 100% identical to the 20P1F12/TMPRSS2 protein of SEQ ID NO:2 (see attached sequence comparison, US-09-323-597b-2.rai) and further includes a fragment wherein valine is at position 160, isoleucine is at position 242, glutamic acid is at position 329, lysine is at position 449, arginine is at position 489, aspartic acid is at position 491.

Conclusion

Applicant's amendment of 2-26-01 (Paper No. 19) necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
May 17, 2001

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600